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Acid-fast Bacteria from Cattle.—A series of white mice were inoculated intraperitoneally with saline suspensions from 8 different strains of acid-fast bacteria, all definitely and consistently acid-fast except one. The organisms used were *M. tuberculosis bovinis*, *M. tuberculosis hominis*, 2 strains of *M. tuberculosis avium*, *M. phlei*, Daines strains 24–0–30 and 38–0–30, and Hastings's strain GH. Daines strains were isolated from a so-called bovine skin lesion and strain 38–0–30 was inconstant as to acid-fastness, and was usually chromogenic. Hastings's strain GH was obtained from a mesenteric lymph node of a cow that failed to react to tuberculin. Each mouse received 0.25 cc. of a suspension slightly more turbid than tube 10 of the MacFarland nephelometer, and 2 rabbits were injected intravenously with 1 cc. of suspension of each organism. Six mice died before 41 days, and the remainder were killed at 94 days. The rabbits died between 2 and 12 weeks. In the rabbits, bacteria obtained from genuine cases of tuberculosis and considered as *M. tuberculosis* induced morbid changes in practically every animal, while no lesions were demonstrable in rabbits receiving injections of the other organisms. The only gross lesions of a tuberculous nature occurred in a few mice in each group that had been injected with true known tubercle bacilli. No microscopic evidence of disease was produced by *M. phlei* or the 2 cultures obtained from Daines. The kidneys of 5 of 6 mice injected with Hastings's strain GH showed largely a histiocytic interstitial cellular reaction only. Organisms were recovered on culture of tissue suspensions from the organs of only those mice injected with tubercle bacilli. The other organisms were nonresistant to reagents which ordinarily have little effect upon the tubercle bacillus. These observations seem to indicate that the bacteria studied, other than the tubercle bacilli, possess features in common with the saprophytic acid-fast organisms, and, although they have certain cultural and biological differences, their failure to produce convincing evidence of pathogenicity should make one cautious in subscribing to their aetiological significance in producing spontaneous disease.—*Observations on Certain Unidentified Acid-fast Bacteria Obtained from Cattle, W. H. Feldman, J. Am. Vet. Med. Assn., February, 1936, lxxxviii, 166.*—(*L. F. B.*)

Johne's Disease.—Paratuberculosis made its appearance in this country probably more than 25 years ago, and thus far no great effort has been made to eliminate it, although it is a serious menace to the cattle industry. The disease is very insidious in onset, and the period of incubation may vary from a few months to several years. Early, there is some loss of appetite, without fever. As the infection advances, the animal gradually loses flesh, and this is associated with more or less intermittent watery diarrhoea. So far as known, treatment is of no avail. The disease is spread by direct transfer of the affected animal. As in avian tuberculosis, the predominant lesion is found in the intestinal tract. In these 33 states, it was diagnosed in 151 herds. In one important dairy State, 13.5 per cent of

906 cattle reacted when tested for the disease. Although a variety of biological preparations were used for testing, in all but two, avian tuberculin or johnin was applied. It is recommended that, where the disease is found in a herd, the infected animal be slaughtered and, if the herd is extensively infected, the entire herd should be slaughtered. Since 1928 the Department of Agriculture has been able to coöperate with stock-owners under a plan similar to that followed in tuberculosis eradication. A number of States have made possible the payment of indemnities to owners of diseased animals. Since the disease is a serious menace and a plan for combating it is established, there should be no good reasons for delay in attacking the problem in earnest.—*Johne's Disease, a Menace to the Cattle Industry, A. J. DeFosset, J. Am. Med. Assn., March, 1936, lxxxviii, 352.*—(*L. F. B.*)

Blood in Rabbit with "Yersin" Type of Tuberculosis.—The "Yersin" type of tuberculosis is produced in rabbits by the intravenous inoculation of either avian or bovine tubercle bacilli. There are two clinical types: One is characterized by death from shock in ten to twelve days; the other produces a sudden, cachectic death in animals apparently in good health, in about three weeks. In this study the blood picture was identical in animals inoculated with either bovine or avian tubercle bacilli. An anaemia, beginning about the fifth day, becomes pronounced between the eighth to fifteenth days, even reaching as low a point as twenty-eight per cent haemoglobin. At this time the temperature rises. This is accompanied by anisocytosis, polychromatophilia and the appearance of nucleated red blood corpuscles. When the temperature begins to fall, announcing approaching death, there is a slight paradoxical tendency to amelioration. But this lasts only a few days, when the animal develops a marked anaemia just before death. In the case of the animals dead of shock, this grave anaemia does not have time to develop. The leucocytic response is in the form of a marked increase in monocytes, as high as 60 per cent in some cases. This monocytosis which is accompanied by a moderate lymphocytosis develops in about the third stage of the disease, coinciding with the elevation in temperature, diminution of red blood corpuscles, drop in haemoglobin and loss in weight. At the same time, in the monocytes there appears such signs of toxic degeneration as vacuolated cytoplasm, and split and multilobed nuclei. This seems to indicate the existence of grave intoxication in animals which do not die of shock with this "Yersin" type of tuberculosis. This monocytosis goes hand in hand with the formation of a large number of epithelioid cells in the spleen.—*Etude hématologique chez le lapin au cours de la tuberculose de type Yersin, M. A. Domanski, Compt. Rend. Soc. Biol., May 23, 1936, cxxii, 385.*—(*M. T. W.*)

Blood of Tuberculous Chickens.—The cellular elements and haemoglobin were studied in 8 adult female Rhode Island Red chickens, between 2 and 3 years of age. Attempts to obtain cultures of *M. tuberculosis* from the blood were unsuccessful with only a single exception. Subcultures of the organisms obtained from a single day's specimen proved pathogenic for rabbits and chickens, but not for guinea pigs. All the chickens had reacted positively to avian tuberculin a few days before they were purchased. Postmortem examination showed characteristic tuberculous lesions in all but one chicken. In two, the lesions were limited to the lungs and in five the disease was extensively distributed. In only three were foci located in the bone-marrow. The erythrocyte counts and haemoglobin were within the limits of those noted in normal chickens, as were the thrombocyte counts. Haematological findings were normal on the bird that reacted to tuberculin but which showed no tuberculous lesions at necropsy. Two chickens with slight disease showed a total leucocyte count higher than normal, with the percentage of heterophils and monocytes increased, and the percentage of lymphocytes decreased. Three of the four chickens with extensive disease showed a marked leucocytosis. The chief increase was in the heterophils and monocytes. One of the four showed a mild leucocytosis. The most striking haematological finding in chickens with tuberculosis was the leucocytosis. This was roughly correlated in a direct ratio to the extent of the disease. Anaemia was not present.—*Chickens with Spontaneous Tuberculosis, C. Olson, Jr. & W. H. Feldman, J. Amer. Vet. Med. Assn., July, 1936, lxxxix, 26.*—(*L. F. B.*)

Acid-fast Bacteria and Bumblefoot of Chickens.—There are few references in the literature regarding acid-fast organisms in tumefactions of the feet of domestic fowls. Acid-fast bacteria, of a size and shape suggestive of *M. tuberculosis avium*, were found on smear in from 45 of 76 cases of bumblefoot. Several fowls with foot lesions did not react to avian tuberculin. With one exception, material from lesions failed to produce disease, when injected intraperitoneally, into chickens, guinea pigs, rabbits and mice. No growth resulted when ma-

terial was cultured upon Dorsets' egg medium. The aetiological relationship of this unidentified organism cannot be stated at this time. It may be a secondary invader or, if a primary invader, it must be of low pathogenicity.—*Acidfast Organisms Found in So-called Bumblefoot of Chickens, H. Bunyea, J. Am. Vet. Med. Assn., March, 1936, lxxxviii, 386.*—(*L. F. B.*)

Anatomical Divisions of Lower Lobe of Lung.—Disease processes of the lower lobe of the lung tend to occupy superior or inferior divisions of the lobe. There is a sound anatomical basis for this. The superior and inferior divisions of the lower lobe have entirely separate bronchial systems. In the embryo the bronchus to the upper divisions of the lower lobes develops from an *Anlage* distinct from that of the rest of the lower lobe. In the adult there may be partial or complete separation of these two divisions by an interlobar fissure when normal fusion has failed to take place. Four-lobed lungs have occurred, in which the fourth lobe corresponds to this superior division of the lower lobe. Pneumonic processes of the lower lobes most frequently involve the superior division. These have often been called "central pneumonias," because roentgenograms taken with the diaphragm low show a process relatively high in the chest. With the diaphragm only moderately low the involvement appears to occupy the lower half of the chest. If the diaphragm is high, the process may be mistaken for encapsulated fluid. Regardless of the position of the diaphragm, lateral views will disclose the posterior location of the process. Such a finding should suggest its anatomical location in the superior division of the lower lobe. The lower division may also be separately involved. When this occurs, the shadow of most of the involved area is masked by that of the liver. This area is frequently involved by post-operative atelectasis. The superior division of the lower lobe of the lung is bounded by the interlobar fissure, between the two main lobes, and by an imaginary line drawn from the hilum backward and downward to the 8th rib posteriorly. In the roentgenogram it appears as a triangular area, posteriorly situated, and with its apex at the hilum.—*A Study of the Lower Lobe of the Lung, J. Levitin & H. Brunn, Arch. Int. Med., April, 1936, lvii, 649.*—(*C. L. D.*)

Alveolar Epithelium.—This is a further contribution to the old dispute whether the alveolar lining cells are epithelial or histiocytic cells. Histological studies were made on lungs showing various degrees of stasis and inflammation and the behavior of the lining cells was observed. The conclusion was reached that it is impossible to demonstrate an epithelial lining in the alveoli. Under certain inflammatory conditions the macrophages simulate epithelium. It was demonstrated that staining methods with silver are not suited to differentiate histiocytic and epithelial cells; it is not true that only epithelial cells can be stained by such methods. The enormous phagocytic power of the large intraälveolar exudate-cells is claimed as an important argument against their epithelial nature. They originate from local histiocytes under non-inflammatory conditions and they have a haematogenous origin under inflammatory stimuli; they are then derived from blood lymphocytes.—*Über die grossen Exsudatzellen und über das "Epithel" in der Lungenalveole, W. Firle, Frankf. Ztschr. Pathol., 1935, xlviii, 1.*—(*M. P.*)

Alveolar Pores in Human Lung.—Alveolar pores have recently become of interest because of the possibility that they may be partly responsible for the peripheral spread of particles in the lungs. It has been known for some time that the emphysematous lung is permeable to fluids. The question of the existence of peripheral intercommunications between the respiratory units is very old. Some investigators have even suggested a definite physiological use for what others have looked on as indicative of degenerative change or accident. The present study comprised the examination of 15 human lungs from subjects two years and five months to eighty-two years old. The pores are best seen in thick, well-stained sections permanently fixed in inflation, because they then may be viewed *en face*, the alveolar wall lying parallel with the glass slide. They appear in thin sections as interruptions in the cut alveolar walls, and are thus likely to be overlooked. Well-marked pores were noted in all the material studied. There was a gradual increase in number and size of the pores with age. This increase in the surface area occupied by the pores seems to be related to the increase with age in the total surface of the alveolar walls themselves, which occurs coincidently with the enlargement of the air-spaces. In early life the pores are fairly uniformly distributed over the lung, but in older people they are present in largest numbers in the borders and apices of the upper and lower lobes. Those found in man are similar to those in the lower animals. Their rounded or oval outline, and smooth, evenly curved contours do not suggest artificial tears or breaks. There is some basis for the view that the pores arise as a result of atrophy, often gradual, of the

ground substance within the capillary mesh, beginning at or near the centre, and enlarging until held by the reinforcing fibres close to the capillary. As a rule, pores are rarely seen in the walls of a collapsed lung, and only the largest retain any degree of patency. Their inequality of distribution and age variation refute the suggestion that pores, at least new pores, might be formed as the result of intrabronchial fixation with undue stretching of the ground membrane. Are pores harmful? Do they spread disease? Phagocytes have been observed within the pores, apparently passing through them. It is possible that phagocytes carrying living bacteria, such as *M. tuberculosis*, might so spread infection and disease, though it must be admitted that about tuberculous and similar foci there are inflammatory reactions which are likely to close the pores. If one admits that the pores are essentially a degeneration, one must look on all advantages which they confer as purely fortuitous.—*Alveolar Pores and Their Significance in the Human Lung, C. C. Macklin, Arch. Path., February, 1936, xxi, 202.*—(*J. S. W.*)

Pulmonary Acinus.—In the terminology of the anatomy of the lung it should be emphasized that those parts of the lung which are supplied by the pulmonary arteries should be called pulmonary parenchyma and the parts supplied by the bronchial arteries belong to the bronchial tree. The anatomical unit of the pulmonary parenchyma is the acinus. There exist important functional differences between the bronchial tree and the pulmonary parenchyma besides the respiratory function. Phagocytosis by local cells occurs only in the pulmonary parenchyma while this function is performed by pus cells in the bronchial tree. Histiocytic cells are practically absent in the alveolar walls, but numerous in the bronchial walls. Following intratracheal injection of vital dyes the covering cells of the alveoli become stained immediately, while following intravenous injection of the same dyes this does not happen. It is concluded that the lining cells of the alveoli are epithelial cells and not histiocytes.—*Über den Lungenacinus, L. Aschoff, Frankf. Ztschr. Pathol., 1935, xlviii, 449.*—(*M. P.*)

Pathological Anatomy of Reinfection and Endogenous Pulmonary Tuberculosis.—Studies on autopsies for thirty-five years show the occurrence of 60 to 65 per cent of reinfections. If, in cases of recurrent tuberculosis there is a later perifocal reaction, it is very seldom of the same intensity and size as seen in childhood and adolescence. The majority of reinfections show a marked tendency to spontaneous healing. A transitional stage into the tertiary form without a perifocal inflammation is characterized by a direct involvement of the peribronchial lymphatics and the bronchus itself, or by an erosion of a blood-vessel. Occasionally multiple tubercles may develop, which proliferate widely into the pulmonary parenchyma. These tubercles, presenting a caseous centre surrounded by lymphocytes and epithelioid cells, may undergo necrosis, and at times destruction of large areas of pulmonary tissue. This type of "alterative cavity" is a cavitation *sui generis* and may be due to a reactivation of an old tuberculous focus, as a result of the disappearance of the symbiotic immunobiological balance previously present in the organism, where there is now a complete absence of tissue resistance against the tuberculous virus. This type of degenerative necrosis about the old focus fails to show any proliferative reaction (Marchand's alteration of the tissue). Such a degeneration in the "alterative cavity" is generally followed by a most favorable condition of the involved interstitial tissue, bronchi and blood-vessels as to the lymphogenous drainage offering a continuous supply of infectious material for the production of metastasis. The formation of an "alterative cavity" is the morphological manifestation of one of the first stages of reactivation of an old focus and probably of the beginning of an endogenous reinfection in the adult. In the author's autopsy material of acute progressive cases of pulmonary tuberculosis, the endogenous development of the phthisis due to reinfection was observed in 24 to 30 per cent. The formation of such a perifocal cavitation, which is similar to a "Schmincke cavity" is sometimes revealed by roentgen examination.—*Studien uber die pathologische Anatomie der Reinfekte und der endogenen Entwickelung der Lungentuberkulose, W. H. Stefko, Schweiz. med. Wchenschr., May 4, 1935, lxv, 401.*—(*F. G. K.*)

Histology of Primary Complex.—These studies were concerned only with old primary complexes. A total of 77 cases were studied. Of these, 39 showed bone-formation; they were all from patients above the age of 40. Bone-formation was found in 66 per cent of patients above 40 years of age. Bone-formation occurs probably only after the tubercle bacilli have disappeared. Parenchymal foci show more frequently bone-formation (72.7 per cent) than lymph-node foci (38.8 per cent), and in the latter the ossification is usually less massive. In lymph-node foci the development of bone-marrow without bone is frequently observed. On the basis

of this observation, it appears likely that ossification starts with the development of bone-marrow from granulation tissue which grows into the foci. The yellow color of the primary foci is due to fat in the capsule. This fatty infiltration may serve the purpose to make the capsule more impermeable for bacilli. The bone-marrow of primary complexes participates in systemic diseases of the bone-marrow. In support of this view, cases are cited in which the bone-marrow of the primary focus showed metastatic carcinoma and metastatic purulent osteomyelitis. Such an occurrence may lead to an exacerbation of the primary focus.—*Beitrag zur Histopathologie der fortgeschrittenen Stadien des phthisischen Primärkomplexes, M. Amorim, Beitr. pathol. Anat., 1935, xcv, 330.*—*(M. P.)*

Pathogenesis of Epituberculosis.—The term "epituberculosis" has been applied to the condition existing in tuberculin-positive children who develop a characteristic X-ray shadow which may arise suddenly or slowly, and which then gradually disappears. The clearing of the shadow requires from several months to a year or longer. The X-ray shadow is usually rather homogeneous in density, and is ordinarily wedge-shaped, with the base of the wedge on the pleura and its apex at the hilum. It may be located in any lobe, and sometimes involves an entire lobe. Its border is often sharply outlined by the interlobar fissure. During the gradual process of clearing, the area becomes progressively smaller, and clearing proceeds from the margins rather than in a spotty fashion. When it does not clear completely, a residuum of strands converging at the hilum may remain for years, and sometimes small foci of calcification remain after the original shadow has disappeared. The symptoms of the disease are mild in comparison to those of progressive tuberculous pneumonia. The temperature is either normal or only slightly elevated. The children may feel very well; occasionally, however, other manifestations of tuberculosis, such as tuberculides, phylctenular conjunctivitis or bone-and-joint lesions may accompany the resolving pulmonary shadow. An X-ray lesion, quite like this so-called epituberculosis, was produced experimentally by introducing dead tubercle bacilli into the bronchi of hypersensitive rabbits. This shadow, which exhibited the form and clinical course of that in human epituberculosis, reached its maximum density in 2 to 4 weeks, and then gradually cleared completely, often beginning at the periphery, as is common in the case of the shadow of epituberculosis. No similar X-ray shadow occurred in nonallergic animals subjected to the same procedure. Immunized, hypersensitive animals, injected intratracheally with living tubercle bacilli, developed a similar shadow, which, however, spread progressively to a fatal termination. The macroscopic appearance of this epituberculosis-like shadow, studied at different intervals, was that of a tuberculous pneumonia which clears by resolution and organization. After resolution, strands of nonspecific scar-tissue may be found at the site. Histologically, the lesion produced is that of a typical tuberculous pneumonia, with epithelioid and giant cells, lymphocytes and caseation. Tubercle bacilli or their fragments could be stained as long as the reaction remained. Later, peripheral organization, absorption of the exudate and nonspecific scar-formation occurred. These findings demonstrate that the peculiar characteristics of epituberculosis can be reproduced by the discharge of dead bacilli into the lung of an allergic individual *via* a bronchus. On the basis of this fact, it is suggested that characteristic epituberculosis represents in many, if not in all, cases the result of erosion of a bronchus by a caseous lymph node containing relatively few viable bacilli; and that the characteristic shadow represents a tuberculous pneumonia produced by the discharge of caseous material impregnated with tuberculoprotein and dead bacilli, though containing some living bacilli, into the lung of a body sensitized and immunized by the previous infection. If a similar accident occurs in the case of a node teeming with live bacilli, a shadow of precisely similar form will develop, but the process will extend progressively. The various and clinically familiar shades between the benign retrogressive wedge-shaped area of epituberculosis, and the wedge-shaped rapidly progressive area of active tuberculosis, may be expected to occur, depending upon the balance between the number of viable bacilli in the discharging node, and the degree of acquired resistance and hypersensitivity of the body.—*Experimental Studies on the Pathogenesis of Epituberculosis, E. H. Oppenheimer, Bull. Johns Hopkins Hosp., November, 1935, lvii, 247.*—*(J. S. W.)*

"Acute Atypical" Miliary Tuberculosis.—Cases of acute tuberculosis presented in their clinical course an indefinite, usually septic, picture, while microscopic examination revealed as actually present a kind of "atypical miliary tuberculosis." There was present also a blood-picture resembling "lymphatic leukaemia," which was assumed to stand in direct aetiological connection with the tuberculous infection.—*"Acute*

Atypical" Miliary Tuberculosis, i.e., without Macroscopically Evident Findings, Cases Showing the Clinical Picture of Lymphatic Leucaemia, F. Harbitz, Acta Tuberc. Scandinav., 1936, x, 59.—(F. B. S.)

Pathology of Childhood-Type Pulmonary Tuberculosis in Adults.—In 19 autopsies on patients between 20 and 45 years of age, a definite relationship between infantile pulmonary structure and the infantile type of the pulmonary tuberculosis has been found. In infantile pulmonary parenchyma there are abundant poorly differentiated mesenchyme cells, and in cases of tuberculosis the mesenchyme reaction is not very definite, while with the normal tissue reaction in adults there occurs a typical productive reaction. Tuberculous involvement during the first years of life is characterized mostly by large area of the lesion, with an exclusively lymphoid type of reaction and a lack of productive response. The cases examined by the author proved the prevalence of the physically hypoevolutive types, which include hypogenitalism, infantilism, dystrophies, and polyglandular insufficiencies. In cases of adult tuberculosis presenting the childhood picture, the hypoevolutive type was seen in 68 per cent, the musculoabdominal type in 16, and the asthenoid-thoracal type in 16 per cent. Anatomically, every form of tuberculosis was observed, but tubercle-formations of the visceral and parietal pleura with injection of the lymphatics and with caseation of the pleura seemed more frequent. While, in most instances, lymphohaematogenous spread was encountered, there were only a few cases in which the infection was spread by bronchogenic means. Cavities were generally very small, showing a thick membrane but no fibrous wall. While in almost all the cases of pulmonary tuberculosis there are definite histological characteristics of the parenchyma consistent with the age of the patient, there is no correlation with age in cases with a persisting infantile type of tissue. The histoarchitecture of the lungs, its differentiation and morphological age determine the character of the pathological process. In the cases of childhood tuberculosis type in adults the exudative reaction is mostly encountered, and dissemination occurs along the lymphatics from both the small focal cavities and the larger confluent ones, and in many cases produces a "lymphostatic pneumonia." Stefko, in a previous paper, maintains that transitional forms between the adult and childhood type of tuberculosis, presenting acinous bronchopneumonic lesions with collateral inflammations and productive acinous lesions are typical of pulmonary tuberculosis in adolescence.—*Pathologische Anatomie der den Kindheitsformen entsprechenden Formen der Lungentuberkulose des Erwachsenen, W. I. Pusik, Ztschr. Tuberk., March, 1936, lxxiv, 426.—(F. G. K.)*

Evolution of Cavities.—There is no tuberculosis which is purely exudative or purely productive but now the one now the other attains prominence in the course of the disease. Ranke's ideas of stages—primary complex, generalization, and isolated organ tuberculosis—are not tenable; nor is there a characteristic type of allergy which is associated with a given stage. Allergy coexists with the entire course of the disease, proceeding in the form of a curve, now exudative, and then productive, hyperergic or anergic. Whenever there is evidence of clinical activity or destructive changes in the lesion, allergy is on the upgrade; when symptoms disappear and the lesions come to a standstill allergy is declining. Occasionally anergy develops, as indicated by negative reactions to O. T. Allergy is the resultant of numerous factors. Among these are (1) biological, (2) age-disposition, (3) perifocal inflammation and (4) exogenous factors. Among the biological factors influencing allergy the author considers: *1: The anatomical structure of the organ* in which allergy develops. In a spongy tissue like the lung exudative phenomena can more readily attain prominence than in a solid organ like the liver. Likewise, the canalicular structure of the lung and kidney favor the dissemination of the disease. Colloidal equilibrium is another of the biological factors operating in allergy. *2: Increased osmotic pressure*, which results from disintegration of protein in necrosis, influences the exchange of fluid between the lesion and the blood. *3: Increased hydrogen ions*, which also attract water to the site of local acidosis, and may influence the motility of leucocytes. *4: Changes in permeability of blood-vessels*, which strongly influence the course of inflammation and the allergic process. Age is an important factor in the course of tuberculosis and the allergic process. Strukow has shown that the lung of human beings undergoes a definite cycle of development. With increased age there is an increase in the number of alveoli at the cost of a decrease in the number of respiratory bronchioles and alveolar ducts. With increased age there is also a decrease in the mesenchyme cells in the lung parenchyma and a reduction of interstitial tissue and lymphatics of the lung. These cyclic changes may affect the character of tuberculosis at different age-periods. Hence, perifocal inflammation is more intense in a

child's lung, for it is afforded greater facility for the diffusion of toxins. Exogenous factors greatly influence allergy. Starvation causes an increase of myelocytes in the circulation, releasing enzymes that may play a part in the softening of old inactive lesions. Klebanow cites the experience of prisoners of war in Siberia, and of excessively malignant caseous pneumonic types of tuberculosis, with massive involvement of lymph nodes and serous cavities, among Austrians, Germans and Hungarians subjected to starvation. The tuberculosis in these Europeans resembled the tuberculosis seen among natives that had never come in contact with tuberculosis. Softening is a thing apart from caseation, and may or may not develop after caseation. Cavities usually form when the allergic curve is rising; and their development is influenced by such factors as architecture of the organ, colloidal equilibrium, etc., as discussed above. But even if the skin is anergic to tuberculin, cavities are at times seen to develop; we have no information in these cases on the reactivity of the mesenchyme of the lung at that time. Cavities may be divided into proteolytic, sequestrating and alterative types. The proteolytic enzymes of the polymorphonuclears are essential in cavity-formation. Hypersensitiveness is responsible for the influx of polymorphonuclears into the softening mass. During the rapid rise of allergy there is a reduction in the resistance offered by the specifically reacting monocytes to the growth of tubercle bacilli. The multiplication of the latter chemotactically attracts the polymorphonuclears, whose enzymes liquefy the caseous material. From this results a proteolytic cavity. The sequestrating cavity results when widespread pneumonic areas of the typical tuberculous variety or of a nonspecific character undergo caseation, and are overtaken immediately by the softening process. Under such conditions, large masses of necrotic tissue are separated, and often float in the fluid of liquefied caseous material. This indicates the height of the allergic process. It often leaves large holes in a normal parenchyma. When old, discrete, encapsulated foci undergo exacerbation and the capsule becomes infiltrated with round cells the *caseum* in the centre loosens and splits off. Leucocytes play little part in this type, the alterative cavity.—*Das Werden der Caverne, J. Fink, Acta. tuberc. Scandinav., 1935, ix, 278.*—(*M. B. L.*)

Stenosis and Perforation of Large Bronchi.—The clinical symptoms and pathological findings of pulmonary lesions following bronchial obstruction demand a differentiation between bronchial stenosis on an anatomical basis and that due to functional disturbance causing a valve-like action. Many bronchiectases result from such a valve-like action interfering chiefly with expiration. The "patho-mechanics" of bronchiectasis should be investigated along this line. Many cases, chiefly in adults, show open cysts and honeycombed pulmonary lesions, and represent the terminal stages of sacculated bronchiectasis. The author would give up the conception of bronchiectasis as based on a congenital development, and he proposes the use of the term "polycystic pulmonary disease" instead of "congenital honey-combed lung." Sometimes haemoptyses originate from enlarged bronchi associated with benign tumors, granulations, mucosal hyperplasias, or from lesions in the neighborhood of tuberculous or anthracotic lymph nodes. Tissue reactions around these lymphatic foci, which are usually associated with a primary tuberculous complex, are characterized by infiltration and perforation of the bronchial wall with partial or complete sequestration of the focus; they lead to bronchostenosis and may give rise to atelectasis and atelectatic pneumonia of the adjacent pulmonary lobe. Those cases, in which there is excretion of tubercle bacilli without demonstrable pulmonary lesion, may be due to perforation of a bronchus without atelectasis. When a bronchus is entirely obstructed by scar-tissue, a persistent lobar atelectasis may result, whereas, with incomplete obstruction, a putrid bronchitis may develop. It seems reasonable to assume that material containing tubercle bacilli and originating from a lymph node can be brought to those areas where aspirated material usually settles by coughing, with the reacting bronchial infarcts and early infiltrates that are characterizing a bronchogenic phthisis. Many areas of an exudative lesion, located chiefly peripherally and showing regression, are probably atelectases rather than tuberculous foci with perifocal reaction. This concept of bronchial stenosis gives rise to a new understanding of many of the problems of pulmonary tuberculosis and may prove of fundamental importance in therapy.—*Stenosen und Perforationen der grossen Bronchien in ihrer Bedeutung fur die Lungenpathologie, F. Fleischner, Wien. klin. Wchnschr., August 2 & 8, 1935, xlviii, 983 & 1016.*—(*F. G. K.*)

New Method of Bronchospirometry.—A new method of bronchospirometry is described, in which a Pflüger rubber cuff is placed around the distal end of a bronchoscope and a Krogh spirometer is attached to

the other end for recording respirations. Two bronchoscopes are used, one of which is introduced usually into the main bronchi and the other ends into the trachea. Both ends of the bronchoscopes are surrounded by rubber cuffs, inflatable by means of two rubber balls, a suitable pressure being determined by a manometer attached. Arrangements are made for determining the CO_2 elimination and the O_2 consumption during the test. The bronchoscopy is carried out under local anaesthesia with 2 per cent pantocain solution. The right lung is shown to have a somewhat larger share in respiration, 53–56 per cent, while the left lung shows 44–47 per cent. Bjorkman found a direct correlation with the weight and total volume of the two lungs. Tests made on subjects in different postures revealed the surprising fact that the compressed lung shows 10 per cent greater respiration and oxygen intake than the upper lung. It may possibly be explained by the fact that there is more thorough pervasion of blood through the lower lung. The utility of bronchospirometry in pathological cases is considered with the description of several cases. In these cases the CO_2 elimination accurately followed the ventilation while the O_2 intake deviated considerably. During bronchospirometry it could be seen that a patient coughs only with his sound lung and for this reason finds it difficult to expel pathological secretions.—*On Bronchospirometry, H. C. Jacobaeus, Acta. Tuberc. Scandinav., 1936, x, 32.*—(*F. B. S.*)

Ascorbic Acid Metabolism in Tuberculosis.—Forty-four cases of tuberculosis, minimal, moderately advanced and far advanced, and in every stage of activity as shown by X-ray, symptomatology, and sedimentation rates, were studied from the standpoint of daily excretion of vitamine C. They were classed in four groups according to the amount of ascorbic acid excreted daily. Vitamine C was determined by means of titration against phenolindophenol. There was a rough parallelism between activity in uncomplicated tuberculosis and the daily excretion of ascorbic acid on a controlled diet. A second method of classification was based on the response to a 4-oz. orange-juice (or 55-mgm. ascorbic acid) supplement to the diet. Those excreting more than 16 mgm. ascorbic acid daily within two weeks after the orange-juice supplement was instituted were considered giving a positive reaction. The positive group comprised 14 cases, of which 100 per cent were inactive cases, and the negative group comprised 10 cases, of which 80 per cent were active. A normal healthy individual requires 15 to 20 mgm. ascorbic acid daily, whereas the tuberculous patient requires 55 to 138 mgm. daily to bring him into equilibrium as regards vitamine C nutrition.—*Ascorbic Acid Metabolism in Tuberculosis, F. H. Heise & G. J. Martin, Proc. Soc. Exper. Biol. & Med., 1936, June, xxxiv, 642.*—(*F. B. S.*)

Action of Lung on Polypeptides.—Isolated and ventilated lungs of narcotized dogs were perfused by Binet and Burstein's method. Citrated whole blood and citrated whole blood plus polypeptides were used for the perfusions. Determinations of the amino nitrogen and of the polypeptide nitrogen were made before, during, and at the end of these experiments. The lungs were perfused for two and a half hours. There was no significant alteration in the polypeptide nitrogen in the citrated whole blood: there was, however, a slight rise in the amino nitrogen. In perfused citrated whole blood to which had been added 2 gm. of polypeptide per litre, it was found that the polypeptide nitrogen fell rapidly. In none of the experiments did the polypeptide nitrogen reach the normal level at the end of two and a half hours. There was a corresponding increase in the amino nitrogen. Citrated whole blood with polypeptides added and incubated at 39°C. did not show such changes.—*Action du poumon sur les polypeptides, L. Binet & M. Burstein, Arch. Med. Chir. l'App. Resp., 1936, xi, 97.*—(*C. L. D.*)

Vitamine D and Serum Phosphatase.—Phosphatase is an organic catalyst capable of either synthesizing or hydrolyzing any mono-ester of phosphoric acid. It is present in large quantities in the intestinal mucosa, kidney and bone. Smaller quantities are found in all other organs and secretions. Determinations of serum phosphatase were made upon normal human beings and upon tuberculous individuals before and after the administration of viosterol. The phosphatase content of normal human serum was found to average 3.31 units in a series of 19 cases. In 32 cases of pulmonary tuberculosis, all stages, the phosphatase content averaged 2.95 units. Twenty-four tuberculous patients were given viosterol, 10,000 X, 1 cc. daily for ten days. The average serum-calcium before the administration of viosterol was 11.8 mgm. per 100 cc. of blood-serum, and after the administration 14.2 mgm. In 14 cases the serum phosphatase was reduced, whereas in 10 there was an increase. Seven of the 11 patients, whose serum-calcium was 14 mgm. or over, showed a decrease in serum-phosphatase content. The changes in the phosphatase titre, however, were apparently within the range as

reported for normal human beings.—*Phosphatase Content of Human Serum in Pulmonary Tuberculosis Following the Administration of Vitamin D, P. D. Crimm & J. W. Strayer, Ann. Int. Med., April, 1936, ix, 1393.*—(*J. S. W.*)

Lipins of Tubercle Bacillus.—Phthiocerol is a constituent of the wax of the human-type tubercle bacillus. It is a higher alcohol, optically active ($[\alpha]_D = 4.8°$), with a melting point of 73–74°. It has the formula $C_{34}H_{67}(OH)_2OCH_3$ or $C_{35}H_{69}(OH)_2OCH_3$. It is different from the higher alcohols isolated from a timothy-bacillus wax or a leprosy-bacillus wax.—*The Chemistry of the Lipids of Tubercle Bacilli. XLVI. Phthiocerol, a New Alcohol from the Wax of the Human Tubercle Bacillus, F. H. Stodola & R. J. Anderson, J. Biol. Chem., 1936, cxiv, 467.*—(*F. B. S.*)

Lipins of Leprosy Bacillus.—Two new alcohols, α and β leprosol, having the formulae $C_{26}H_{46}O_2$ or $C_{25}H_{44}O_2$ and phenolic properties, have been isolated from the unsaponifiable matter of the acetone-soluble neutral fat of the leprosy bacillus. The composition and the reactions would indicate that they contain a benzene nucleus and that a hydroxyl and a methoxyl group are in the ring. There may be one or more side chains, but their nature and position are unknown.—*The Chemistry of the Lipids of Tubercle Bacilli. XLV. Isolation of α and β Leprosol, J. A. Crowder, F. H. Stodola & R. J. Anderson, J. Biol. Chem., 1936, cxiv, 431.*—(*F. B. S.*)

Composition of Leprosin.—A neutral wax-like substance, called *leprosin*, and isolated from the leprosy bacillus, was analyzed, and found to consist of a complex mixture of solid glycerides and waxes. The fatty acids liberated on saponification were myristic, palmitic, stearic, tetracosanic acids and a new hydroxy acid called *leprosinic acid*. The neutral portion of leprosin after saponification consisted of both water-soluble and ether-soluble components. Glycerol was the only water-soluble substance that could be detected. The ether-soluble unsaponifiable matter consisted of two higher, secondary, optically active alcohols. The less soluble alcohol was identified as d-eicosanol-2. A second alcohol, probably d-octadecanol-2, was also isolated. These same alcohols have been previously identified as constituents of the so called wax fraction of the timothy bacillus. Leprosin is acid-fast.—*The Chemistry of the Lipids of Tubercle Bacilli. XLIII. The Composition of Leprosin, R. J. Anderson, J. A. Crowder, M. S. Newman & F. H. Stodola, J. Biol. Chem., April, 1936, 113, 637.*—(*F. B. S.*)

Reactions to Wax-Like Materials from Acid-Fast Bacteria.—The materials in acid-fast bacilli which have the properties of waxes are not waxes in the chemical sense, since no sterols have been found in them. They are really composed of higher alcohols, hydroxy acids of high molecular weight combined with polysaccharides, and occasionally glycerides. Like waxes, these materials are not only completely insoluble in water, but they cannot even be wet with water. These wax-like materials have the property of acid-fastness and contribute it to the bacilli. For convenience, they are nevertheless referred to as waxes. In this paper the cell reactions to bacillary wax is considered in comparison to those previously reported with the phosphatide fraction. Unsaponifiable wax from human tubercle bacilli H37 was injected intraperitoneally into rabbits in three ways: first, as a dry powder through a cannula; second, as a dry powder through an incision under anaesthesia; and, third, in colloidal suspension. The second method proved the most satisfactory for all materials. The colloidal suspensions afforded the opportunity of introducing these inert materials in fine particles. Although the waxes are stable and seemingly inert substances, chemically they are remarkable stimulants for the new growth of cells. Their essential property is that they stimulate the formation of monocytes wherever they lodge in the tissues. These monocytes then fuse around the wax and become foreign-body giant cells. The wax can be identified within the cells by its property of acid-fastness. Only the finest particles of the material, as when introduced in colloidal suspension, are phagocytized by the individual monocyte; rather, the masses of the wax become surrounded by many monocytes which fuse into a giant cell which is at first a hollow sphere. The larger inner surface of this fused cytoplasm is then able to engulf the material. The material remains for a long time within the giant cell in the form of irregular masses, with no immediate tendency toward the formation of particles of equal size so characteristic of the epithelioid type. But in the period of months, typical acid-fastness gradually grows less, until only a diffuse, pink reaction like that of a colloidal suspension remains. On the other hand, the phosphatide, in contrast to the waxes, is readily dispersed in water, making stable suspensions. In water these phosphatides form myelin-like figures, which can be readily identified within the cells. It has been shown that these phosphatides are phagocytized by monocytes and that they are acted upon within the cell in a specific manner. The material is soon broken up into increasingly smaller particles within the cytoplasm. When they become

finely divided, the cell is the typical epithelioid type, indistinguishable from the form seen in the disease tuberculosis. The time necessary for the formation of epithelioid cells ranges from four days to two weeks. Some of the monocytes which have phagocyted the phosphatide become multinuclear, making Langhans giant cells. The end-result, though it may be long delayed, is the death of the cell. The monocyte can readily phagocytose the lipoid and disperse it to a certain state, but it seems not physiologically adapted to a disintegration of the phosphatide (and fatty acid) into its simpler molecular groups. Epithelioid cells then regress, either through the death of the individual cells, or *en masse*, in which case the phenomenon is called caseation. Thus it is seen that the method of dealing with the wax within the giant cells is different from that of dealing with the phosphatide. It is a slower process, and there is nothing that might be compared to the process of emulsification as with the phosphatide, but there is a gradual disintegration of the material until it is too finely divided to give an acid-fast stain. More important still is the difference in the fate of the cell which has taken in the wax. No sign of damage to the cells has ever been detected; they do not disappear through caseation; there is no sign of cell death in the tissues. It is probable that the giant cells eventually separate into single monocytes, although this point is not proved. The first reaction to the introduction of wax in the peritoneal cavity is an outpouring of neutrophilic leucocytes. This reaction does not persist, and in about two weeks time the neutrophilic leucocytes have disappeared from the tissues and eosinophilic leucocytes appear. The latter do not seem to wander into the peritoneal exudate, but rather remain around the giant cell. Their presence is so constant around these lesions that they suggest that the giant cells break some material from the wax which is chemotactic to eosinophiles. An inconstant reaction is the accumulation of lymphocytes around the foci of giant cells. The effect of the material injected intravenously on the course of a subsequent infection with tubercle bacilli indicates that the waxes have no influence on resistance. The waxes are elaborated by the Mycobacteria and give them the property of acid-fastness by which they are classified, but their function is probably in connection with the life and the survival of the bacillus and they induce no reactions in the host which are associated with resistance.—*Cellular Reactions to Wax-Like Materials from Acid-Fast Bacteria. The Unsaponifiable Fraction from the Tubercle Bacillus, Strain H-37, F. R. Sabin, K. C. Smithburn & R. M. Thomas, J. Exper. Med., December 1, 1935, lxii, 751.*—*(J. S. W.)*.

Reaction to Waxes from Leprosy Bacillus.—This study is similar to the immediately preceding one, but deals with the waxes extracted from *Mycobacterium leprae.* The materials used were still in the process of purification, and have therefore provided the opportunity to compare the complex cellular reactions to mixtures of substances with the simple response noted with the highly purified crystalline alcohols. The materials were introduced intraperitoneally as before. All of them contained some substance which gives the formation of the simple foreign body giant cell. With some of the wax-like substances the most striking phenomenon was the formation of large abscesses wherever masses of the wax lodged. These abscesses are not at all like caseation, for there is no basis of dead cells, but rather it is the wax itself which becomes infiltrated with leucocytes. These materials also are irritants, causing a marked dilatation of the blood-vessels and probably a new growth of vessels. They also contain certain substances that are remarkable stimulants for the formation of fibroblasts and of new fibres. Besides all these properties, they contain some material that gives rise to typical epithelioid cells. A glyceride, *Leprosin*, was found to possess two simple properties: It causes a remarkable new growth of fibroblasts and then it stimulates the formation of foreign body giant cells around the particles of wax.—*Cellular Reactions to Waxes from Mycobacterium Leprae, F. R. Sabin, K. C. Smithburn & R. M. Thomas, J. Exper. Med., December 1, 1935, lxii, 771.*—*(J. S. W.)*

Pigment of Tubercle Bacillus.—The regions of selective ultraviolet absorption of phthiocol, the pigment of the tubercle bacillus, dissolved in 95 per cent alcohol were near λ 3850, 3340, 2780 and 2500 Å. The same selective absorbing mechanism seems to be responsible for this absorption as in the case of the naphthoquinones. It is modified by the methyl groups of the phthiocol in the λ 2800 and 2400 Å region and by the hydroxyl groups.—*The Ultraviolet Absorption Spectrum Curve of Phthiocol, a Pigment of the Human Tubercle Bacillus, M. O'L. Crowe, J. Biol. Chem., 1936, cxv, 479.*—*(F. B. S.)*

Experimental Infection of Guinea-Pig Foetus.—The newborn animal is relatively mature in form and function, and reflects in large measure the resistance or susceptibility characteristic of its species. Whether these

characteristics are manifest in the youngest embryos or become gradually apparent during the growth-period to birth is unknown. The foetus occupies a unique situation, being in an environment of constant temperature and nutrition and well protected from chance contamination and external influence. Hence, foetal inoculation offers a new field for bacteriological investigation. Most of the work herewith reported was done on the guinea pig as the most suitable animal. With little experience the approximate foetal age can be judged by palpation. This is possible from about the 20th day of gestation until term at about the 65th day. Several different methods were used, depending on the foetal age. Until about the 30th day the foetus is too small for direct inoculation. For this stage intraplacental inoculation under anaesthesia was employed. Following midline laparotomy the placentas were inoculated by needle-punctures through the uterine wall. The objection to this method is that there can be no control of the distribution of inoculum between maternal and foetal blood-sinuses in the placenta. Foetuses from about 30 to 40 days of age were inoculated intracerebrally by needle-puncture through the maternal uterine wall as above. In fact, most of the experimental work with different inocula were made at this period of gestation and in this way. When it was essential to avoid maternal contamination the foetus was exposed by a small incision through the uterine wall and foetal membranes, and the site of inoculation cauterized to destroy surface traces of the inoculum. Older foetuses were inoculated intracerebrally through small incisions in the maternal abdominal wall immediately over the foetal part desired. Sometimes this can be done through the intact abdominal wall. The termination of the experiments was chiefly by caesarean section. If the mother is allowed to go to term identification is not possible. The following antigens were selected for inoculation in foetal guinea pigs: The virus of poliomyelitis, vaccinia virus, the submaxillary gland virus of guinea pigs, tubercle bacilli H37 and *BCG*, and diphtheria toxin. Embryonic tissues have been found particularly favorable for the propagation of many viruses in tissue-culture. In these experiments with the foetal guinea pig there were marked tissue changes and often death following infection by the tubercle bacillus and submaxillary-gland virus. The histological changes produced by vaccinia virus were less extensive but death often resulted. Although foetuses were killed by small amounts of diphtheria toxin there was little gross change. The poliomyelitis virus was inert. It may be that foetal reactions, like those of adults, will be found to be individualized, with respect to both host and parasite.—*Direct Bacteriological Experimentation on the Living Mammalian Fetus, O. C. Woolpert, Am. J. Path., March, 1936, xii, 141.*—*(J. S. W.)*

Intracerebral Inoculation of Foetal Guinea Pigs with *BGC*.—Calmette has stated that his vaccine is a *virus fixe* permanently attenuated and incapable of regaining its former pathogenic properties under any environmental conditions. Whenever it has been alleged that the vaccine had regained virulence or caused progressive tuberculosis, Calmette and his supporters have claimed that there had been a contamination of the inoculum or an intercurrent infection of spontaneous origin. Woolpert has developed a technique by which foetuses may be inoculated *in utero* without interruption of the gestation period. Such a technique is particularly applicable to the problem of *BCG*, since the foetus is protected from exposure to intercurrent infection. The remote possibility of transplacental tuberculous infection obtains only when the mother has an overwhelming infection. The foetus may be more susceptible than young or adult animals to relatively avirulent organisms and may constitute a favorable medium for passage experiments in attempts to convert *BCG* into a more virulent form. Before investigating *BCG* in this manner, the reaction of the guinea-pig foetus to a standard virulent strain of tubercle bacilli was determined in order to establish a basis for judging the results with *BCG*. A series of foetal guinea pigs was inoculated intracerebrally, according to the method of Woolpert, with graded doses of strain-H37 tubercle bacilli, and, if not dead, were killed at the end of a predetermined length of time, and then examined grossly, histologically and bacteriologically. The dosage used varied from 0.01 to 1.0 mgm. The results indicated that H37 establishes in the guinea pig foetus a progressive tuberculosis in certain respects similar to that produced by this bacillus in the adult animal. A larger series of guinea pig foetuses was then inoculated with graded doses (0.01 to 3.0 mgm.) of *BCG*, and the effects compared with those obtained with the virulent tubercle bacilli (H37). Both types of tubercle bacilli were found to spread from the site of inoculation, but not with equal rapidity; with the same dose, it took a longer time for the *BCG* to cause as much disease in the foetus, as a whole, as did H37. Pathologically, the response of the foetus to both organisms was the same, although somewhat larger doses of *BCG* were administered in most instances. A few of those

receiving the smaller dosages of *BCG* manifested no evidence of tuberculosis. Many of the *BCG* animals that were permitted to be born naturally died of generalized tuberculosis or showed extensive tuberculous changes when killed. There was definite histological evidence that *BCG* is capable of multiplying in foetal tissues and of initiating a disease process different only in degree from that produced by H37. Attempts at foetus-to-foetus transfer of *BCG* were not successful. Recovery of this bacillus on artificial media from inoculated foetuses was accomplished four times in twenty-four attempts.—*Intracerebral Inoculation of Fetal Guinea Pigs with Bacilli Calmette-Guérin and the H37 Strain of Tubercle Bacillus, I. S. Neiman & O. C. Woolpert, Am. J. Path., March, 1936, xii, 153.*—(*J. S. W.*)

Experimental Tuberculosis of Brain.—Apropos of Boquet and Broca's work, showing tubercle bacilli in the brains of rabbits infected intravenously, studies were made to determine the presence of tubercle bacilli in rabbits and guinea pigs infected by various methods with human or bovine strains. Nineteen guinea pigs were infected subcutaneously. The brain was cultured. Only 4 positive cultures resulted, showing a rare colony. Numerous colonies resulted from cultures of the brains of 4 guinea pigs inoculated intravenously. Eight rabbits were inoculated intravenously, intrapleurally and intracutaneously. One positive result was obtained out of two rabbits inoculated intravenously. Negative results were obtained in each of two rabbits inoculated into the pleura. Two out of four produced positive results of the rabbits inoculated intracutaneously.—*Recherche des bacilles tuberculeux dans le cerveau apparemment sain des animaux tuberculeux, R. K. Goyal, Compt. Rend. Soc. Biol., January 18, 1936, cxxi, 223.*—(*M. T. W.*)

Experimental Intestinal Tuberculosis Following Inoculation into Mesenteric Lymph Nodes.—Since the ordinary methods of inoculation of tubercle bacilli do not provoke the formation of intestinal lesions, an attempt was made to establish lesions by an analogous retrograde mechanism. Tubercle bacilli, human, bovine and *BCG*, were inoculated into the mesenteric lymph nodes of guinea pigs on a level with the ileocaecal angle. Small disseminated nodules were found in the mucosa of the intestinal wall in the animals which died three to five weeks later. In guinea pigs which received a smaller dose and died four to eight weeks later, a thickening of the intestinal wall at the level of the ileocaecal valve was found. At this spot the folds of the mucosa were less prominent than normal and covered with micronodular lesions. Elsewhere the intestinal wall was dotted with hard nodules, sometimes containing caseous pus. A very small dose of bacilli produced, after a considerably longer time, much the same type of lesion; only it was larger and sometimes ulcerated. There seemed to be no difference in infections in animals which had been vaccinated with *BCG* subcutaneously or into the lymph nodes. The intestinal walls in the ileocaecal region in every case showed slight thickening.—*Détermination expérimentale de lésions tuberculeuses intestinales chez le cobaye par l'inoculation de bacilles dans les ganglions mésentériques; inoculation de BCG dans les memes ganglions, J. Beerens, Compt. Rend. Soc. Biol., May 16, 1936, cxxii, 272.*—(*M. T. W.*)

Tuberculosis of Bones and Joints in Rabbits.—Slowly progressive tuberculosis produced in rabbits by the intracutaneous inoculation of minute quantities of highly virulent bovine tubercle bacilli is regularly associated with tuberculous lesions in the bones and joints. These lesions originate by extension from the bone-marrow and result from haematogenous spread. They gradually invade the bony tissue and end as cold abscesses under the periosteum or within the joints. Both in their localization and development they are comparable to the bone-and-joint tuberculosis seen in man.—*Caracteres anatomique des lesions tuberculeuses osseuses et articulaires, obtenues chez le lapin par inoculation de bacilles bovine, A. Boquet & R. Laborts, Rev. Tuberc., April, 1936, ii, 440.*—(*M. B. L.*)

Serological Diagnosis of Tuberculosis in Guinea Pig.—A positive complement-fixation reaction in tuberculosis does not indicate the presence of specific antibodies but results from the tissue disintegration of the tuberculous process. Animals which have acquired a high degree of specific resistance show few if any antibodies in the serum. The concentration of these antibodies is inversely proportional to the degree of immunity. In general, the antibody concentration is higher in those instances in which the destruction of tissue is greatest. The significance of complement fixation in man can be elucidated by the analysis of this reaction in experimental animals. Witebsky-Klingenstein and Kuhn's method is still more reliable than the Meinicke reaction in the diagnosis of tuberculosis in the guinea pig. The concentration of these antibodies in inoculation tuberculosis of the guinea pig is lower than in active tuberculosis of man.

Only after several months' duration of the disease do antibodies appear in the guinea pig's serum.—*Die Serodiagnose der Tuberkulose in Meerschweinchenserum und ihre Bedeutung für die tierexperimentelle tuberkuloseforschung, P. Weiland, Ztschr. Immunitätsforsch., May, 1936, lxxxviii, 104.*—(*M. B. L.*)

Effect of Ferric Chloride on Tuberculous Rabbits.—Rabbits previously immunized with *BCG* and then inoculated with a virulent bovine strain of tubercle bacilli (Ravenel) survived 44 to 144 per cent longer time if they were given intravenous injections of ferric chloride (0.25 per cent) over a period of 16 weeks. Five independent series of experiments during five years, using over 100 rabbits, showed these results. Iron is deposited in tuberculous areas, and iron pigment, indistinguishable from haemosiderin is found intracellularly in the spleen, liver, and bone-marrow. In one series of experiments a group of control tuberculous but nonimmune animals succumbed at a very early stage. The results therefore show that dilute ferric chloride intravenously administered definitely retards the progress of tuberculosis in experimentally infected rabbits. Preliminary clinical application is reported.—*A Summary of Studies on the Effect of Ferric Chloride on Tuberculous Rabbits, V. Menkin, Proc. Soc. Exper. Biol. & Med., March, 1936, xxxiv, 262.*—(*F. B. S.*)

Protective Action of Copper in Rat.—Rats could be infected with 0.1 mgm. of a virulent "Ravenel" bovine tubercle bacilli, and revealed gross lesions in the lungs in three to five months. When copper sulphate, in amounts equivalent to 0.2 mgm. of copper per rat per day, was added to the standard diet containing 0.025 mgm. of elemental copper per 15 gm. of food, the rats showed marked resistance to tuberculous infection. When 2 mgm. of elemental iron per rat per day was added to the diet in the form of iron-ammonium-citrate, the tuberculous infection was increased.—*Protective Action of Copper against Infection with Mycobacterium Tuberculosis (Bovine) in Albino Rats, D. Perla, Proc. Soc. Exper. Biol. & Med., 1936, April, xxxiv, 365.*—(*F. B. S.*)

Cultivation of Tubercle Bacilli.—Cultural examination for the primary isolation of tubercle bacilli was carried out in 2 series, which included all the routine specimens received at the Central Laboratory, Ontario Department of Health, during 1933 and 1934. For 1,826 specimens, Petragnani's, modified Petroff's and Woolley's media were used routinely. Dorset's and modified Dorset's media were tried, but found inferior, and their use was discontinued. Of the 3 media used, Petragnani's yielded the greatest number of positive results. On 642 specimens, the cultural examination was controlled by animal inoculation. Cultures were obtained from 105 specimens, while 88 produced typical tuberculosis in animals, inoculated with 1.5 cc. of the treated sediment. For 2,329 specimens, Loewenstein's medium, with and without sodium silicate, Petragnani's medium, and Woolley's medium, with and without glycerine, were used throughout the series. Feldman's medium was tried, but was not as satisfactory as the others, and was discontinued. Of the media, Loewenstein's gave the most positives, of which 74.2 per cent were visible in four weeks. In a further comparative study of cultures and animal inoculations on 629 specimens, the animals gave positive results for four more specimens than the cultures. The animals were inoculated with 1.5 cc. of the untreated specimen.—*Cultural Methods of Isolation of Tubercle Bacilli, A. L. MacNabb, Am. J. Pub. Health, June, 1936, xxvi, 624.*—(*E. R. L.*)

Comparison of Culture Media for Tubercle Bacilli.—It has been stated that the presence of blood in culture media for Koch's bacilli is detrimental to growth. With this in mind a few studies were made with the media of Besredka, Kirschner and Beck-Proskauer. Flasks of broth of all three media, with and without blood, were inoculated with 0.01 and 0.0001 mgm. of tubercle bacilli and incubated for forty-five days. Growth was first visible on Kirschner's medium and continued to be more rapid; then it appeared on Besredka's medium, and finally on Beck-Proskauer's. The addition of blood had no effect on growth, neither favorable nor inhibitory.—*L'influence du sang humain sur le développement du bacille de Koch dans les milieux de culture liquides, A. de Carvalho & C. Vidal, Compt. Rend. Soc. Biol., January 18, 1936, cxxi, 265.*—(*M. T. W.*)

Colony Morphology of Tubercle Bacilli.—The hydrogen-ion concentration of the medium on which tubercle bacilli are grown may have a profound influence on the colony morphology of these organisms. For a study of this phenomenon, 25 strains of tubercle bacilli were grown on glycerolated egg-yolk (with congo-red), whose pH ranged from 6.0 to 7.4. The bacilli included 3 avian, 12 bovine, and 10 human strains of various ages. Marked variation in colony topography of organisms grown at various pH values occurred in 18 strains in the first generation. The remaining 7 strains (all

human type) showed similar changes in the second generation. With the avian tubercle bacilli, smooth variants, whether derived from virulent or avirulent strains, were produced over a broad range of pH; the rough variants appeared only on the more acid medium, and even then not to the exclusion of smooth forms. The bovine bacilli produced three variants instead of two, as in the case of avian organisms. The more granular forms occurred most abundantly on the more acid medium (pH 6.0), the smooth forms on the mid-range of pH, and the third variant, designated intermediate, was produced almost to the exclusion of other forms on neutral or alkaline medium. Organisms grown at pH 6.0 were least readily suspensible, those grown at pH 7.2 somewhat more readily, while those at pH 6.4 and pH 6.8 were in general much more readily suspensible. The human strains produced variants similar to those of bovine bacilli. In the case of the bovine organisms, however, the optimum range of pH for smooth colonies was pH 6.4 to 6.8, whereas among human strains large numbers of smooth colonies occurred only at pH 6.4. The pH range for intermediate variants of human tubercle bacilli was therefore slightly broader than with bovine organisms. The observations were made by the time the cultures had been incubated for one month, as with prolonged incubation, which allows for secondary growth, the influence of pH control becomes less evident. Included among the avian and bovine strains were organisms of widely varying pathogenic properties. Virulent and attenuated strains of a given type produced similar colony variants under similar environmental conditions. It is apparent that a delicate mechanism operates to determine both colony form and virulence of tubercle bacilli. If the factors of that mechanism are controlled so that maximum numbers of smooth colonies are produced, then greatest virulence is retained. The bacilli, when grown on more acid medium, produce fewer smooth and greater numbers of rough colonies and suffer attenuation. Sensitivity to alkaline medium is less, so that still another and but moderately attenuated colony variant is produced. This may be the reason why the pH range most suitable for the development of intermediate colonies does not occur between those values which are more suitable for R and S variants. It is possible that with some other culture medium than glycerol-egg yolk the pH values optimum for certain colonial variants might be quite different from those observed in the present study.—*The Colony Morphology of Tubercle Bacilli. V. Influence of the pH of the Culture Medium on Colony Form (with two plates), K. C. Smithburn, J. Exper. Med., 1936, lxiii, 95.—(J. S. W.)*

Mutation of Tubercle Bacillus.—From a nonchromogenic culture of human tubercle bacilli of slight virulence, yellow colonies were observed when the culture was grown upon Kumbary's medium or when emulsified in ferric-chloride solution and cultured. During a period of two years, 20 generations of the culture have shown chromogenesis, and at no time were nonchromogenic colonies observed. From this chromogenic culture the authors obtained dry R colonies and moist S colonies. While the R variant not infrequently changed to S, the reverse of this was not true. The R variant appeared on solid media as flat, wrinkled colonies, and on liquid media produced a wrinkled heavy surface growth with no clouding of the media. The culture was not easily emulsified and the suspension was unstable. The S variant formed rounded, smooth, soft, slimy colonies, and grew diffusely throughout liquid media with the formation later of a fine thin surface film. These colonies were readily emulsified, forming a stable suspension. The chromogenic culture grew only at 37°C. Animals injected with this culture reacted four weeks after infection to 1:10 or 1:100 dilutions of Old Tuberculin. When injected into guinea pigs the R variant remained sharply localized, and produced enlargement of the regional lymph nodes with occasional nodules in the internal organs. On the other hand the S variant showed a greater tendency to spread by way of the lymphatics and blood-stream. Neither the R or S variant nor the original culture produce progressive lesions when injected into animals. Rabbits and mice injected with these cultures did not show progressive lesions. The culture could be reisolated from the organs of the infected animals as late as four months after inoculation.—*Ueber die pigmentbildende Varietät des Tuberkelbazillus, J. Weissfeiler & L. G. Kalinina, Zentralbl. Bakt., January, 1936, cxxxv, 475.—(J. D. A.)*

Changes in Biological Properties of Human Tubercle Bacilli.—The fact has been demonstrated that human tubercle bacilli, forming typical R colonies, and isolated from animals inoculated with human products, and treated with the acetone extract of Koch's bacilli, have special characteristics. For instance, some tubercle bacilli thus obtained have marked pathogenicity for the rabbit while others obtained in the same way show only feeble virulence for the rabbit. After several reseedings on artificial medium these strains lose their

pathogenicity for the rabbit in the same manner in which smooth strains of tubercle bacilli isolated by the same method. Eventually they behave like tubercle bacilli of typical human variety. The passing pathogenic properties of these bacilli for the rabbit have been shown not to be attributable to the action exercised by the acetone extract. The hypothesis that the tubercle bacilli are chance invaders from the outside has also been excluded by experimental work. It has likewise been demonstrated that bacilli forming R colonies, isolated by the acetone extract method from the blood of guinea pigs previously inoculated with a known human strain of tubercle bacilli, present in most of the cases an increased pathogenicity for rabbits exactly like the bacilli obtained by the same method from pathological human material. These organisms likewise lose their virulence for rabbits after a few seedings on culture media. But in two cases the strains carried for three years continued to remain virulent for the rabbit after inoculations of 0.01 mgm., while the original strain failed to infect rabbits when given in even larger doses. These two strains produced lesions in the rabbit exactly like tubercle bacilli of true bovine strain. In consequence, an attempt was made to determine the exact character of these strains. They grew abundantly on the differential potato medium containing bile while the original strain did not. However, they reacted to Sauton's medium to the same pH degree as did the original strains. Intrapleural inoculations were made into rabbits in accord with Boquet and Laporte's work, in an attempt to further classify these atypical strains. But here again they behaved like bacilli of human type. Thus, two strains of tubercle bacilli producing R colonies and isolated from the blood-stream of tuberculous guinea pigs treated with the acetone extract of Koch's bacillus were found, which after several years continued to behave in some respects like the human type but retained their pathogenicity for the rabbit.—*Sur la transformation de certaines propriétés biologique de bacilles tuberculeux de type humain insolés du sang de cobaye par l'extrait acétonique de bacilles de Koch, L. Negre & J. Bretey, Compt. Rend. Soc. Biol., January 25, 1936, cxxi, 279.*—(*M. T. W.*)

Dissociation of Acid-Fast Bacteria.—Cummins and Williams recently isolated an acid-fast organism other than Koch's bacillus, called the "m" strain, from the sputum of a girl suffering from chronic pulmonary illness. A similar organism, called the "I. P." strain, was isolated from the sputum of a patient seen by Baldwin, the patient presenting a clinical picture almost identical with the above. An attempt was made to dissociate these strains and to compare the behavior of the variants on artificial media; also to determine whether they possessed any pathogenicity for laboratory animals. A third strain, a nonpathogenic acid-fast organism isolated from a *BCG* culture was included in the study. Each strain was dissociated into at least two variants possessing distinct topographical and other biological characteristics. Some of them in the early stages of colony development appeared to be white, but as they aged, when left at room temperature and exposed to light, they invariably developed chromogenicity. All grew at 37.5° as well as at 20°C.; however, at the higher temperature their growth was more profuse. Their morphological and tinctorial characteristics could not be used in differentiation. Non-acid-fast forms could be demonstrated in very young and again in older cultures. They were all very pleomorphic. These studies definitely show that environmental conditions play no small part in morphological variation. The organisms were nonpathogenic for laboratory animals except in the case of "M", which displayed some pathogenicity for mice and rabbits. It may be that larger doses are required, or it is possible that their virulence will be enhanced after several animal passages. They were weak antigens, producing complement-fixing antibodies with some specificity. Specific tuberculins could be prepared from each strain, and animals inoculated with the strain reacted more strongly to homologous than to heterologous tuberculins. The interpretation of the significance of the various so-called nonpathogenic acid-fast organisms isolated from human sources is at present still a speculative one. It seems, however, that we cannot regard them merely as saprophytes, although there are certain similarities, such as their behavior on artificial media, production of chromogenicity, pH curves, and pleomorphic morphology in different environments. It seems highly probable, however, that these organisms may, under certain circumstances, be responsible for the production of disease in man.—*Dissociation of Two Unusual Acid-fast Organisms Isolated from Human Sources, W. Steenken, Jr., & A. Landau, J. Infect. Dis., May-June, 1936, lviii, 247.*—(*J. S. W.*)

Dissociation of Bovine Tubercle Bacilli.—It has been shown that bovine tubercle bacilli belonging to the S dysgonic variant may be dissociated into an R eugonic strain by repeated transfers on potato-glycerine medium, a phenomenon that takes

place in various ways. Sometimes the strain progresses slowly and with difficulty from the S type, becoming eugonic in character very gradually and only after repeated transfers. At other times the transition is produced abruptly, rough eugonic colonies appearing on the surface of a smooth colony. The dissociation may also appear on dysgonic cultures allowed to remain in the incubator for several months. These R colonies, recently isolated and transplanted to egg-medium, give rise to apparently smooth and glistening colonies, but at the same time difficult to emulsify. Among these colonies certain ones remain dysgonic; others become small and somewhat pigmented but, when transplanted back to potato-glycerine medium, all become R variants. The R variants are unstable both *in vivo* and *in vitro*. Some bovine strains do not lose their smooth, dysgonic characteristics.—*Dissociation du bacille tuberculeux de type bovin, R. Laporte, Compt. Rend. Soc. Biol., October 26, 1935, cxx, 399.*—(*M. T. W.*)

R and S Chromogenic Acid-Fast Bacilli from Leprous Lesion.—R and S forms of acid-fast bacilli were obtained from an acid-fast dull yellow bacillus isolated from a subcutaneous leprous nodule according to the method of Duval. The R form grew more rapidly, formed a flaky suspension, was more thermostable, showed a predominance of large bipolar granules, and was surrounded by a thicker capsular zone. The R and S forms are reversible, the S being the typical and the R the mutant form.—*Biological Study of "R" and "S" Forms of Chromogenic Acid-fast Bacillus from Human Leprous Lesion, J. K. Kriz, Proc. Soc. Exper. Biol. & Med., 1936, April, xxxiv, 303.*—(*F. B. S.*)

Tubercle Bacilli with Attenuated Virulence.—Of 35 strains of tubercle bacilli isolated from cases of lupus, 19 were of the human type, 12 of the bovine type and 4 atypical; 86 per cent of all strains showed attenuation. Five more attenuated bovine strains isolated from other forms of tuberculosis are also described. Probably more attenuated strains were found than are usually reported because the direct method of cultivation was used in addition to the primary inoculation of the original material into guinea pigs. Because of the marked attenuation of virulence of the bacilli in cases of lupus, a very careful examination of the virulence is recommended for determining types of strains. The attenuation in rabbit virulence is accompanied by a similar attenuation in virulence for guinea pigs. The conclusions put forward are in confirmation of those by A. S. Griffith.—*Studies on the Types of Tubercle Bacilli Isolated from Man. II. Strains with Attenuated Virulence, K. A. Jensen & J. Frimodt-Möller, Acta Tuberc. Scandinav., 1936, x, 83.*—(*F. B. S.*)

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